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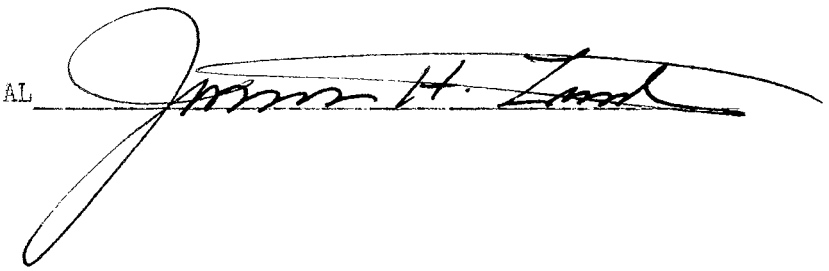
Scope of Study: Facts concerning mutations, the recent findings in this area of biological science, and the many ramifications of mutations and their effects have not been and are not now common knowledge to teachers of biology and other sciences. Many teachers of science in high schools suffer a deficit of knowledge in this area of science. Most biology textbooks do not adequately cover this aspect of genetics and many which do are outdated. The purpose of this report is to present some of the more important facts and concepts of mutation so that any person with a minimum of science for a background can understand more about this biological phenomenon. The report strives to give the partial explanation of mutation causation as indicated in the literature which was surveyed, and to show how mutations may affect man. This report is not intended to be a technical scientific report, but rather a general over all report that can be understood easily by any person having a small amount of scientific knowledge.

ADVISOR'S APPROVAL 

MUTATIONS: THEIR CAUSES AND EFFECTS.

by

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TABLE OF CONTENTS

LIST OF FIGURES

Chapter I

INTRODUCTION

Mankind has long wondered and pondered over the question of what makes him exactly the creature he is. People today can only imagine how ancient man must have been bewildered by this puzzle.

By means of written history, the modern world has a record of the wonderings and questionings of some of the later peoples. To some of this present age, the theories and ideas presented by means of such history are quaint and perhaps funny. To some, this history, of the progression of ideas concerning what it is that makes man, and all other organisms, have the characteristics they have, shows very clearly the pattern of the formation of our own modern concepts of genetics and related subjects.

Because of man's natural interest in this subject and the stimulation which has been provided by some earlier workers, much work, experimental and written, has been done in the study of genetics, and the related field of mutations. The purpose of the report is not so much to present all of the material that has been produced on the subject, but rather to present some of the material, selected and prepared so that a satisfactory knowledge of the subject may be gained. This is done in order that the writer, as a teacher, may easily communicate with future students in this subject.

The writer intends to review some of the history behind our present-day concepts of mutation, to discuss briefly some facts and theories of

the modern viewpoint in such a manner as to be useful in teaching high school biology, and show how mutations affect man in a few respects. It is hoped that the reader will keep in mind at all times, that the primary purpose of the material presented is that it be useful in the writer's future teaching experiences.

As a starting point, some early work of such men as Lamark, Wallace and Darwin have been selected. It is thought that these early concepts and opinions are important because they help to point out the development of modern concepts.

The problem of explaining the phenomenon of mutations was extremely hard until the recognition of the gene as the unit of hereditary transmission. It was found that the gene was the agent in which changes of hereditary material took place. Later another important step was made when the gene was recognized as the primary unit of mutation as well as segregation, crossing over, and physiological reactions.

As the influx of knowledge increased, greater advances were made, until man was able to induce the biological changes, or mutations, artificially. With this ability man was able to begin to explain why mutations occured, or, in other words what caused them. It is with this problem that the second area of the report deals.

But first, listen to the words of two men, concerning man's position as far as the explanation of mutation is concerned. H. J. Muller, first to induce mutations with X-rays said,

> "Although the radiological attack has yielded a massive body of information relating to chromosome and gene structure, our ignorance in the area far exceeds our knowledge."[1]

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[1]Gabriel and Fogel, Ed., Great Experiments in Biology(Englewood Cliffs, 1955), p. 261.

One of our staff members Dr. Lynn Gee, says,

> "At the present state of man's knowledge of genetics, there is no 'Unified Theory' to explain the mechanisms even in such a comparitively simple organism as the bacterial cell."[2]

In discussing the section of modern concepts and theories, the writer is more concerned with the causative factors of mutations than the reasons behind the causation. This is due, primarily, to two reasons. One, the number of ideas and amount of work done in this area is so great, the writer would not be able to adequately present all factors pertaining to mutations, and therefore must be selective in the amount and kind of material to be used. Two, the fact that the paper is of an introductory nature prohibits coverage of all aspects of the problem of mutation.

In the last section, the writer has presented and discussed a few mutations of economic importance to man; in other words, those which affect him indirectly through his domesticated plants and animals, and those that affect man directly through his own heredity. In considering these mutations that affect man, both harmful and beneficial ones are to be studied.

[2]Biological Principles and Concepts for High School Science Teachers (Stillwater, 1957), pp. 21-13.

Chapter II

HISTORICAL DEVELOPMENT

Scientists today attempt to explain the evolving of the various species by the phenomenon mutation. Even though the scientific world is not settled on a unified Theory of Mutation it may be generally said that this explanation is done by the use of the Mutation Theory. Credit is given, and justly so, Hugo DeVries as the father or founder of our modern Theory of Mutation. However much effort and time had been expended by men before the time that DeVries did his work in the field. It is the opinion of the writer that an understanding of some of these earlier efforts is necessary to obtain the greatest benefit from our modern method of explaining the evolution of species.

Even though this report does not delve into the actual transformation of species, the reader is urged to be cognizant that a study of such transformations is important. Since most work of a historical nature dealt mainly with forming of new species it is necessary that some historical information be given.

A Frenchman, Lamark, gave an early opinion or theory, as to the formation of new species. This man contributed to many fields of science other than biology. It is in the field of biology, and in particular his theory of the evolution of new species for which he is best remembered today.

Lamark believed a number of things which have since been proven false. As an example of this, he believed firmly the theory of spon-

taneous generation, and also that it took place not only in early development of life, but at all later periods down to his day. Lamark surely knew of Spallazani's experiments which disproved the theory of spontaneous generation of maggots yet refused to accept this evidence.

Lamark had his own ideas about generation. Life, he believed, could be produced by both organic acts and by nature herself, without any act of this kind. By this he meant that some bodies, without possessing life, could be prepared to receive it.[1]

The thing for which Lamark is best known, is what the scientific world today looks upon as another untruth. Lamark believed that organisms inherited aquired characteristics from their ancestors. He believed that man's special organized condition was due to gradual aquistion of characteristics over a long period of time while conditions were favorable to bring about these changes.

Since Lamark's Theory dealt primarily with inheritance of aquired characteristics instead of spontaneous variation or mutation, the question, What might aquired modifications be? needs to be answered. Two kinds have been described; those due to enviroment alone, and those modifications which arise from either a lesser or greater degree of use or disuse depending whether an organ was gained or lost. This last type, alone, Lamark regraded as a factor of evolution. Here, then, is the basis for Lamark's theory that each successive organism is more complex than it's parents. If the organism failed to use a particular organ, that organ would tend to atrophy due to it's disuse. If it used a particular organ more than usual, the organ would tend to become larger,

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[1]A. S. Packard, Lamark, His Life and Work, (New York, 1901), pp. 156-158.

stronger. Either case he felt, was a gain in complexity. Lamark also believed that these aquired characteristics were passed on to future offspring.

Lamark's arguments seem reasonable in a way. Moles or cave fish, not using their eyes, after a time lose the use of their eyes. Snakes have lost their legs because their mode of life dictated they didn't need legs. The intestine of drunken humans is shortened because they consume less solid food. Since there is less work for it to do, it has decreased in length. Giraffes have aquired long necks, because in times past their ancestors had to stretch their necks to obtain food. The ones which could stretch the longest survived and passed this characteristic to their offspring.[2] Thus argued Lamark, but it has been demonstrated that his theory does not satisfactorily explain the origin of new species.

Darwin had the following to say about Lamark.

> "Heaven forfend me from Lamark's nonsense of a tendency to progression and adaptations from slow willing of animals. But the conclusions I am led to are not widely different from his; though the means of change are wholly so."[3]

The voyage of the Beagle was the most important determinant of Darwin's career as a naturalist. It was from information gained on this voyage around the world that he wrote his Origin of the Species by Natural Selection. Darwin's theory is commonly called the Theory of Natural Selection. Lamark believed that change came about solely because of use or disuse of an organ. Darwin placed his confidence in believing that the environment was primarily the causative factor

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[2]Elliot, Hugh, Tr., Zoological Philosophy, by Jean B. Lamark, (London, 1914), p. xliii.

[3]Packard, A. S., p. 731.

in the change of the species. In other words the direct influence of the environment upon the individual or species was more important than any use or disuse upon the part of the organism. Many people think that Darwin's theory was one which said that man had descended from monkeys. It is the writer's opinion, in view of information from the reference materials, that this is not the case.

The theory of natural selection may be broken down into several component parts. These are 1) Over production, 2) Struggle for existance, 3) Hereditary differences, 4) Survival of the fittest.

It has been estimated that a termite queen lays more the 30,000,000 eggs a year. Some species of fish lay several million eggs at a time. If all individuals lived to maturity they would soon overpopulate the earth.

Over reproduction causes a struggle for existance. This does not mean struggle for existance in usual manner such as a desert plant struggling to get water. Rather it indicates a struggle for existance between members of the same species. Since such individuals would need the same substances to live, if there is not enough to go around, some must do without.

Hereditary variations means that some organisms are better adapted to live in a given environment. In time of extreme duress, those best fitted will survive, and the others will die. The surviving members will produce offspring and pass on the characteristics needed to survive in that environment, while those that die will produce no offspring and the weaker characteristics will be eliminated from the species. Thus the organisms best suited for survival in that environment are naturally selected.

Such a pattern of development would require a length of time to complete its course. Many people held to this view point, but evidence today is that the changes of a species come about suddenly and not by a slow gradual change due to ordinary variability. The idea of rapid, sudden and discontinuous changes, as the formative factors of new species, came with the postulates given by Hugo DeVries. It was not until DeVries did his work in the field of mutations that the true significance and importance of mutations were discovered.

Both Lamark and Darwin attempted to explain the formation of a new species as a long drawn out series of affairs. In general the major causative factors were the environment and the organism's need to adjust itself to the environment as it changed. Over a long period of time the organism would have changed enough to be considered as a new species.

DeVries had a different idea and solution to the problem. He seemed to think that the new species were formed by mutation. DeVries thought that a mutation was a transition of a given character of an organism which changed very suddenly, rather than gradually, and which continued to breed true. In his attempt to fully explain this, he indicated that three types of mutations existed. As a result the following types were listed by him.

A. Formation of new characters: Progressive specific mutation.
B. By existing characters becoming latent: Retrogressive specific mutation.
C. By activation of latent characters: Degressive specific mutations.[4]

As one might conclude, DeVries' Theory of Mutation was very closely connected with his ideas of the origin of the species. The information which he has given us has been the foundation upon which much of the

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[4]DeVries, Hugo, The Mutation Theory, Vol II,(Chicago,1910), pp. 71-72.

present day work has been based.

He felt that no parent transmits its characters as an inseperable whole to its offspring. Rather, by a process of change, a small or large group of characters or a single character is passed on to the offspring so that it differs from its parents in only a small point. When a new species originates, it is not the whole nature of the organism which changes. It is rather a change only in one or two points, while everything else remains in a static state.

DeVries indicated that hereditary characteristics were caused by or composed of elementary units. He made an analogy to molecules as the elementary units of a chemist. He was quite aware of the fact that these units could not be analysed as could the chemical ones, but by his Theory of Mutation he attempted to explain them. His Theory of Mutations, explaining hereditary characters composed of fundamental units, complied more fully with existing sciences, such as embryology. Most all prior conceptions had been based almost entirely upon the theory of selection; however the usefullness, and thereby the recognition of a theory, rests largely upon its suggestiveness and the number of facts which it explains. It was the usefullness of DeVries' theory which made it so common place and popular.

The Theory of Mutation lays much stress upon sudden and discontinuous changes while Darwin considered these and his theory of selection in the origin of new forms, and A. R. Wallace went to an extreme, saying that changes come about only by slow gradual changes, Both Darwin's and Wallace's theories have not proved productive as has DeVries'. The other theories had some points which could not be upheld, or which were actually disproven. As example, the Theory of Pangenesis as put forward

by Darwin. He supposed there were small particles or bodies called pangenes, which were produced by all parts of the body. Arm pangenes from the arms, leg pangenes from the legs, etc. These broke loose at the proper time and floated through the blood stream to the sex cells where they were transmitted to the offspring. Before continuing, the range of validity of this Theory of Mutation should be examined.

The validity of the Theory of Mutations can be stressed by bringing to light several points. First of all, the degree with which the Mutation Theory has been used by scientists, and the manner in which it explains the natural phenomena pertaining to it. All available evidence points toward mutations as the primary factor influencing changes in organisms. This is emphasized by findings of researchers during DeVries time and in periods following. In explaining adaptations, the Theory of Mutations has been more useful than any pertaining to natural selection. Natural selection holds basically to the idea of fluctuating variablity, whereas explanation of adaptations requires almost unlimited variability, as can be explained by mutation. The theory of natural selection with fluctuating varialility cannot account for all adaptations which require variations in all directions. Natural selection acts like a sieve which eliminates those inferior organisms incapable of surviving in an environment, but it does not explain how the differences between individuals arose in the first place. Again, natural selection cannot explain the insignificant beginnings of new characteristics, as can mutations, because many of these new characteristics are of no significance in the struggle for existance. Lastly the theory of natural selection, although explaining the existance of useful characters cannot and does not explain those of useless or harmful nature as does the

Theory of Mutation.[5]

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[5]DeVries, Vol II, pp. 598-614.

Chapter III

MUTAGENIC EFFECTS

With an understanding of how the term mutation and it's meaning came about, it is time to examine the mutations themselves. Mutations with all their ramifications, present a complicated study: what causes them? What effects do they cause? Where is the site of their action? Is there any way to overcome mutations? These and many other pertinent questions could be asked. It is the writer's intention to consider some of these questions in coming sections.

Scientists have come to recognize two seperate and distinct kinds of mutations. These, the chromosomal and the gene mutation, differ in site of action and effects produced. Both occur naturally, and experimentally, the range or percentage varying under different circumstances.

As the name might indicate, chromosomal mutations are those which affect the chromosome. Sometimes a chromosomal mutation might affect only a part of a chromosome, sometimes a whole chromosome, and sometimes even a whole set of chromosomes. One type chromosomal mutation is a trisomic. This occurs in an organism having one extra chromosome, the general formula is $2N+1$. The extra chromosome is transmitted through the female parent because an extra chromosome in the male gamete acts as a gamete lethal. This type is present in both plants and animals, but occurs in greatest numbers in plants. A second type chromosomal mutation is monosomic. In this case the organism has lost a chromosome and its general chromosomal formula is $2N-1$. A type in which whole sets differ are called polyploidal. Instead of having the diploid construction

the organism has 3, 4, or even more sets of chromosomes. This kind is prevalent in plants but fairly uncommon in animals. The simple rearrangement of a chromosome, may under certain conditions behave as a mutation. A break in a chromosome at the right place may cause the chromosome, that had borne genes for recessive characters to suddenly behave as a dominant. Two of the more common types of chromosomal rearrangement are inversion and translocation. Inversion is a simple reversal of a chromosome segment. When this occurs, a chromosome breaks in two regions, and the central portion exchanges ends and establishes new connections. This phenomenon causes considerable looping and twisting of the chromosome such that the presence of an inversion in an organism can be demonstrated best by the examination of a cytological preparation of such an individual.

Translocation also involves the breaking apart and reestablishing of a chromosome segment. Translocation differs in that a portion of a chromosome breaks off and then attaches itself to another chromosome. The most common type of translocation involves exchange of materials between non-homologous chromosomes. Translocations can be demonstrated by a cytological preparations, as are inversions.

The last chromosomal mutation to be discussed here is the one caused by position effect of the genes. The discoverers of the gene thought that the gene had no relationship with the chromosomes. In fact a group of early investigators came to the conclusion that the position of the gene in the genetic system was of little importance.[1] However scientists know today that a type mutation called the postion effect is caused by a changed spatial relationship between the genes.

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[1]Dodson, Edward, Genetics (Philadelphia, 1956), pp. 168-178 .

The other type of mutation, gene mutation, is the type in which geneticists are primarily interested. This type mutation has been defined as a permanent change in a gene, causing a new characteristic in offspring which breeds true, and as such, is the basis for both genetics and evolution; of genetics because different alleles of the same gene may be studied in breeding experiments; of evolution because inheritable changes are the only way of explaining the action of natural selection in the differintiation of species. Genes and their corresponding charters are a part of a closely integrated body. Therefore any genetic change, mutation, is very likely to affect many seperate parts of the organism, and therefore likely to have many effects on the species. It should be remembered that genes do not produce their effects as isolated elements. Each gene is not related to a seperate characteristic, but rather when a gene is changed, it is very likely to cause widespread changes in the organism as a whole. Often one hears the expression the gene for curly hair, or the gene for brown eyes. These expressions should not be taken literally, for instead of each gene representing a specific part of the body, the genes as a group determine the development of the organism from fertilization till death.[2]

Mutations have been known for hundreds of years, as shown by records of taxonimists and stock breeders. These breeders often killed their mutants, called sports, so that no one would think they had an impure breeding line. With a rise of the understanding of the significance of mutations, people have tried to explain how or why mutations occur. Two of the more commonly accepted theories mentioned here are to be dis-

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[2]Sinnot, Dunn and Dobzhansky, Principles of Genetics (New York, 1950), pp. 406-407.

cussed later. First is the ionizing or target theory. This one merely explains gene mutations by means of an ionizing process at the gene location, caused by a close or direct hit of a high energy or ionizing particle. The second theory is that of the formation of peroxides on or near the gene which causes the change in the gene, which change is called a mutation. Indeed, there seems to be some indication that the two are closely related in causing gene mutations.

The two types of mutations which have been discussed were classified according to the site of action. One might say that there are two other types of mutation, induced and spontaneous. These are classified according to the nature of the mutation.

Spontaneous mutations were the only type known until around 1927. This was the case because it was not until that date that man was able to induce mutations in organisms. Spontaneous mutations are the natural type; they arise in organisms that have not been subjected to any mutation causing treatment. A single mutant is usually found among large numbers of unchanged individuals and it has probably been changed in only one or two minor points. Saying that this type mutation is spontaneous is tantamount to admitting lack of knowledge of the real causes of the mutation; even today there is not complete agreement as to the cause of spontaneous mutations. It has been suggested that these natural mutations are due to natural short-wave radiations. Investigators have shown that the amount of natural radiation is so small that it could account for no more than one percent of the spontanuous mutations that arise. Some of these same researchers have proposed a target theory. This theory says that a mutation is caused by an ionization or excitation of a gene. However there is still a diversity of opinion among authorities in the

field as to the exact cause of these spontaneous mutation.

The rate of spontaneous mutations cannot be established to the satisfaction of all concerned. Some authorities say that between 5 and 10 percent of the individuals of a species carry a newly arisen spontaneous mutation.[3] W. P. Spencer has said that the total number of mutations exhibited by the Genus Drosophila would be in excess of 100,000. An average of mutation is more applicable than any single mutation. Hence it is estimated that the general average of mutation in Drosophila is about one mutation in every 100,000 gametes.[4] The mutation rate is not easily established since most of the mutations that occur are so insignigicant as to easily escape even the trained eye.

Until 1927, all attempts at inducing mutations artifically had failed. In that year both H. J. Muller and Stadtler confirmed each others reports of inducing mutations by use of X-ray. Muller, working with Drosophila, found that the frequency of mutations in progeny of treated flies was much greater than the rate of spontaneous mutations. Stadtler found the same thing to be true for the irradiation of barley plants.

Muller found that the treatment of sperm from Drosophila caused the occurance of true gene mutations. He assumed that if an equal rate of mutation occured in all chromosomes treated, that about every other sperm cell capable of producing a mature individual held a detectable mutation in at least one chromosome. Muller showed in this and later experiments, that many of the changes produced by X-rays were the same kind of changes which occured in the spontaneous mutations. This was a boon to researchers in the field, for now they no longer needed wait

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[3]Sinnot, Dunn, and Dobzhansky, p. 287.

[4]Dodson, Edward, p. 158.

until a mutation appeared naturally. He recognized very early that induced mutations could be influenced by other things, some of which will be discussed later.

H. J. Muller indicated that induced mutations are dependant upon a change that was initiated in an individual atom, by it's ionization or other excitation.[5] He also thought that the failure of chromosomes to heal, and the gross rearrangement of the chromosomes could be caused also by X-radiation.

Two other investigators, Demerec and Latarjet, were able to induce mutations in Escherichia coli using X-rays and ultraviolet light. They give no theory as to causation but they did find that the highest rate of mutation obtained was about 2.8 mutations/100 survivors.[6]

Muller received the 1946 Nobel prize in medicene for his work in inducing mutations. That work is important enough in the study of mutations that it will be summarized here. Muller not only selected a suitable mutagen, but by restricting his study to sex-linked lethal characters only, he obtained a suitable method of determining the rate of formation of a given class of mutation. He used a ClB stock to obtain the latter. The C stands for an inhibitor crossover in the X chromosome, the l for a lethal recessive, and the B for a bar eye gene which made visible the flies which carried the marked chromosome. ClB females then carry one ClB and one normal X chromosome. Muller irradiated males to produce mutations in the sperm and these were mated with the above females, a pair to a vial. All female offspring must have an X chromo-

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[5]Muller, H. J., "Induced Mutations in Drosophila," Cold Spring Harbor Symposia on Quantatative Biology, 1946, Vol. 11, p. 49.

[6]Demerec, E., and Latarjet, R., "Induced Mutations in Bacteria," Cold Spring Harbor Symposia on Quantatative Biology, 1941, Vol 9, p. 151.

some from each parent. If the sperm is normal, the offspring of these females will be in the ratio of 2 females to 1 male; if the sperm is mutated, she will produce all daughters. This is so because 1 of the ClB is lethal when ever there is only one allele present. This is the case of the males since they posses only one X chromosome. By this procedure, Muller was able to indicate the number of mutations from the proportion of females producing only daughters.

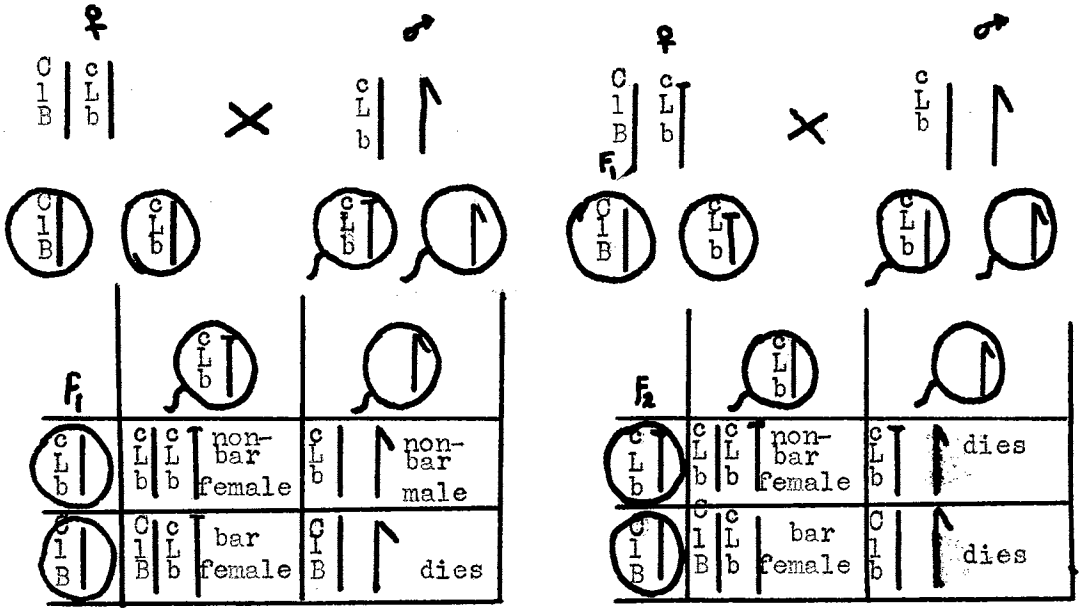

Fig. 1. Diagram of the ClB Method for Detecting Lethal Mutations Produced in the X-chromosome in Drosophila.

The rate of mutation from this experiment is as follows: with 1000r units of radiation, the rate of mutation increases 3 per cent. With 2000r units, it increases to about 6 percent, and with 4000r units it increases to about 12 percent.[7]

Hollaender reports that one X chromosome in 600 contains a lethal gene that has arisen naturally. Contrastingly, if a heavy dose, 5000r

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[7]Dodson, Edward, Genetics, (Philadelphia, 1956), pp. 163-164.

units, of radiation is applied to mature spermatozoa, about 14 percent of the X chromosomes would contain an induced mutation. This is an increase of over 85%.[8]

The early work done in the field of mutations has been discussed; the words mutagenic and mutagen have been used without actually defining them. A mutagen is any substance or thing which can induce a mutation in an organism. Mutagens range in nature from the high energy rays and particles through chemical substances to changing of physical surroundings, or some mechanical change. It is the writer's purpose, now to discuss these different causative factors seperately.

A report given by Hersh, Karrer, and Lummis,[9] gives some basis for belief that high frequency vibrations might possibly affect the mutation rate in Drosophila. Male flies were subjected to vibrations having a frequency of 285,000/second, for 25 seconds. Flies subjected for longer periods of time were overcome and did not revive. The males were then mated, and 26,135 flies resulted as progeny. Among the flies the investigators found a total of 52 abnormalities not usually inherited in Drosophila. Although these data show that the supersonic vibrations had a small effect upon the flies, they do not have the same effects as do X-rays or some other mutagens.

The effect of temperature on the mutation rate had been observed from an even earlier time than Muller's work with X-rays. As a matter of fact, it was Muller himself who showed that more mutations occur in

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[8]Hollaender, Alexander, Ed., Radiation Biology (New York, 1954), Vol. 1, p. 407

[9]Hersh, Karrer, and Lummis, American Naturalist "An Attempt To Induce Mutation in Drosophila Melanogaster By Means of Supersonic Vibrations," 64(1930), pp. 552-559.

A culture of Drosophila that is kept at a higher temperature than normal. He found that increasing the temperature by 10 degrees C., more than doubled the mutation frequency. More recent investigations along this line, indicate that sudden exposures to either extremely high or low temperatures will greatly increase the mutation rate. It is the opinion of most authorities, however, that more work must be done along this line before any definate conclusions can be drawn. The evidence now at hand indicates that the effects of cold and heat upon the mutation rate have a more contributive nature than causative. In other words, under the correct conditions, excessive heat or cold may increase the effectiveness of some radiational and chemical mutagens.

W. R. Horlacher, then of Texas A & M College, conducted experiments which indicated that electricity probably could cause mutations in Drosophila. In his first test, he treated a number of males with 30,000 volts, with time intervals varying from one to thirty minutes. A total of 172 daughters of the treated males were mated, but no lethal mutations were observed. Horlacher observed the F_2 generation for visible mutations and found a white eyed female in one culture, which was a mutation. He also found several peculiarities in wing shape and size; an example is a blister wing of one female. These data were so inconclusive that he conducted a second similar experiment two years later. His findings of this experiment were so inconclusive that he concluded that electricity, at least the type he used, was a very poor mutagen if at all.[10]

Types of radiation, X-ray being the best known, are still the best known types of mutagens. From the time of Muller's first successful ex-

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[10]Holacher, W. R., An Attempt To Produce Mutations By Use of Electricity, Science, 72(1930), pp. 96-97.

periment with X-rays in 1927, many people have devoted themselves to the problem of finding other mutagens. Radiations, of the X-ray type, are the most used and most successful mutagens that have been thus far discovered, and the literature of Genetics is loaded with reports and papers which have been given on X-rays and mutations; hundreds of books have been published dealing with the subject. The work which has been done with X-rays definately proves them to be mutagens, but scientists still do not understand the mechanism behind such mutations.

Prominent geneticists are becoming cognizant of the danger of uncontrolled use of X-rays as a medical tool. They feel that over a period of years a person who receives numerous X-ray treatments may receive enough radiation to cause harmful mutations. They therefore advocate the use of protective shields over the reproductive organs when X-ray therapy is administered. This would stop the radiation which would otherwise cause the mutation. The following discussion, since X-rays have been treated, will be limited to other radiational mutagens.

As early as 1930, work had been done with ultraviolet light as a means of inducing mutations. In that year, sex-linked lethals in Drosophila were induced by radiation of this type. In the next two years, further experiments resulted in the formation of visible mutations in the same species. From then until 1940, much work was done, resulting in mutations in both plants and animals. Generally, in the Genus Drosophila, ultraviolet mutations were similar to those of a spontaneous nature.[11] It seems that ultraviolet affects the chromosomes also, as well as the genes, and a number of scientists have found that ultraviolet, when applied after X-rays, causes a reduction in the number of mutations as

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[11]Hollaender, Alexander, pp. 531-532.

compared with material treated only with X-rays.[12] Scientists attribute this to the fact that ultraviolet prohibits the process by which the broken ends of the chromosomes join to form new combinations.

The induction of mutations, using ultraviolet, has been most successful in small organisms such as bacteria and molds. This is because ultraviolet does not have the power to penetrate thick tissues as does X-ray. For the same reason, it need not be considered as an important source of mutation in man, but it may furnish information as to how mutations are caused.

As indicated, X-rays have been used to induce mutations in all types of living matter; from simple organisms like bacteria and protozoa to the higher animals and plants. It has been shown experimentally that all wave lengths of radiation are effective in forming mutations. The "Hard" gama rays, or those which are emitted by decaying radioactive materials, have been used as mutagens. These rays come chiefly from natural radioactive isotopes found in soil, air, water, and living organisms. This means that all living organisms are constantly being subjected to this type radiation. As far as scientists have been able to determine the dosage from these sources is so small, about 0.11 r/year, they tend to be insignificant.

Another possible source of induced mutations is cosmic rays. These rays have tremendous penetrating power into living tissue, but our atmosphere seems to filter out most of them, so that at sea level, cosmic rays deliver less than 0.08r/year. Cosmic rays were thought to be a serious deterant to space travel, but from all indications the danger

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[12]Ibid.

of suffering harmful effects from these rays is not so great as was thought.

A great many other forms of radiation such as neutron bombardment have been used to induce mutations, but none of them have been as fruitful as X-rays. These forms of energy have been used experimentally in order to study mutations, and worry need not be given them as dangerous to the human race because of mutations they might cause. The one exception is the continued ignorant use of X-ray by some unthinking physicians. Most people receiving such X-ray treatment are past the age of reproduction, or because of the illness are not likely reproduce. People who can be expected to reproduce, should especially be given proper shielding of the reproductive organs so that they will not undergo a harmful mutation.

Responsible physcians and other scientists have shown conclusively that large doses of radiation will cause radiation sickness. This may cause disability or even death. They point out that there is no danger of radiation sickness in carefully regulated exposure, but it is recognized, that there is no minimum dosage known which is needed to induce mutations. Since radiation is such an important tool in medicene and industry, proper precautions must be taken to protect the reproductive organs from as much radiation as possible.[13]

A source of mutation causing radiation, fusion and fission weapons with their radioactive fall-out, has caused a great deal of concern among many genetists. A number of studies have been made concerning the survivors and their offspring, of the Nagasaki and Hiroshima atom bomb

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[13]Dodson, Edward, pp. 164-165.

blasts. The amount of radiation received by these survivors ranged from zero to 700r. . The latter figure is the largest amount of whole body radiation a person can receive and still survive. The initial data from these studies indicates a small effect upon the sex ratio and possibly the frequency of stillbirths. No other defects, due to the blasts, have been noted.

These data, though, are incomplete and many scientists fear we are poisoning our atmosphere by seemingly almost continuous tests of atomic weapons. Some of the radiation given off by each explosion remains in the atmosphere for long periods of time, so that the radiation there is continuously building up to a level, alarming to some. An important fact is that no minimum dosage is known for the production of mutations. Thus each increase in the radioactive materials in our atmosphere, could very likely cause a large increase in the number of mutations in man.

This common knowledge has led to the formation of a group of people calling for the complete cessation of all nuclear tests, while another group maintains they are necessary for the good of the country.

Both arguments, as presented by these people, seem, to most genetists, to stretch the truth not a little. Those arguing that the radioactivity produced from testing atomic weapons is entirely harmless or that nuclear tests be banished altogether, have lost sight of the issue at hand, or perhaps they hope to gain something as yet unseen by most others. True, such radiation may cause mutation, for no dose is so small that it does not carry a risk of causing mutations. It is essential that as many mutations as possible are inhibited from being formed. Over 99 percent of all mutations are harmful to the organism in which it occurs; each

mutation that occurs, continues from generation to generation, until it appears in an individual and causes at least a disability.[14] It is estimated that each survivor of the Japanese blasts transmitted one mutation above the natural number to their offspring. If this occured in each generation, the effects would soon be disastrous. On the other hand, if atomic tests are banned altogether, what is to stop other Nations from producing an atomic weapon with which to conquer this nation? These ideas must be taken into consideration, regulations to govern necessary tests made and methods devised to protect the population from any harmful mutation thus caused.

Many experiments have shown there is little difference in the effectiveness of different wave lengths in causing mutations. Timing experiments have been performed which show that doses of radiation seperated by intervals of weeks had the same mutagenic effect as the total dose applied all in one treatment. Other experiments have shown that weak, long-continued doses had the same mutagenic effects as strong brief treatments delivering the same dose.[15] In general, radiation is a tool, useful in many circumstances; radiation used foolishly may be a terrible instrument of destruction. To repeat, controls must be put into effect which will protect the population from any induced mutations which might arise from the uncontrolled use of such radiation.

A great deal of work and study has been done in the field of chemical mutagenetics. Many chemical substances have been subjected to tests to determine their effect in producing mutations. A number of substances,

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[14]Muller, H. J., Genetic Damage Produced by Radiation, Science 121(1955), pp. 837-838.

[15]Hollaender, Alexander, pp. 531.

including nitrogen mustard, ethyl urethane, phenol, and formaldehyde have been found to posses such an effect. In many cases the studies conducted, consisted of immersing the reproductive organs in a solution of the substance and then transplanting the organ back into the organism. The offspring were then studied for induced mutations.

It has been reported that some chemicals, methycholanthrene and dibenzanthracene as examples, which produce cancer experimentally, also are capable of inducing mutations.[16] Some think this supports the theory that mutations play a part in causing cancers.

All attempts to induce mutations chemically failed, prior to 1947. In that year Charlotte Auerbach succeeded in producing mutations using mustard gas as a mutagen. A number of types of materials and methods were used in the experiment. Using Drosophila as the subject, the mutagen was applied by feeding, by vapour treatment of adults, by immersion of eggs in the mutagen, and by injection into both larva and adults. The feeding technique produced the largest number of mutations, however these were not as reliable as those obtained by treating the adult males.

The first chemical substance to show definate mutagenic properties was mustard gas. The resemblance of X-ray burns and mustard gas burns, plus the inhibitory effect of mustard on the process of mitosis, led to the discovery of the gas as a mutagen. Treatment of Drosophila adults resulted in about 35 times as many lethal mutations as occured in the normal control group. The action of mustard gas in such a role has been confirmed by a number of well-known scientists. Later experiments, the data from which are as of yet incomplete, indicate that the mustard

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[16]Winchester, A. M., Heredity and Your Life, (New York, 1956) p. 231.

gases may produce a substantial increase of mutations in higher animals.

Mustard gases also resemble X-rays in other respects. Auerbach found that the proportion of visible mutations to lethal mutations was approximately the same for both. As might be expected, they differ in many respects, but their similarities indicate that there might be a relationship as to the function of the two agents as mutagens.

Auerbach's experiments showed that a number of other chemical substances were mutagenic. The most spectacular, after the mustard gases, was formaldehyde. Several vesicants, other than mustard gas, showed negative results in mutation induction.

A striking fact is that several mutagens were found to act as carcinogens, or as cancer producing substances. It had long been thought that cancer was produced by somatic mutation, and these data seem to indicate that this is the case. A parallelism of carcinogenic and mutagenic effects of X-rays has been demonstrated, and the newer information that some chemical mutagens may act as carcinogens, adds greater emphasis to the belief that cancers are caused by mutations. However, proof that a few weak mutagens may act as carcinogens, does not make a fool proof connection between mutation and carcinogenesis. Further tests and additional data are needed to make such a connection.

Auerbach found that of the chemical mutagens, a group of toxic visicants, including mustard gas, are the most powerful. Of these chemicals, mustard gas and nitrogen mustard produce results very similar to those produced by X-rays.

Auerbach indicates the belief that chemical mutagens are controlled by a transfer of energy. This transfer of energy occurs directly between

The mutagen and the chromosome affected.[17]

Another important group of chemical mutagens are the organic peroxides. The theory of peroxide formation has come to be as fundamental as the ion theory of mutation activity. However, researchers in the field are of divided opinion as to which of these theories is the better in explaining the phenomena which occur during the process of mutation. Only time will tell which of the two is better, and perhaps a combination of the two will provided the best explanation.

In 1949, F. H. Dickey conducted an experiment, on a pure strain of bacteria, dealing with organic peroxides as mutagens. The basis for these experiments was the knowledge that bacteria grown on a recently irradiated culture plate, showed a high percentage of mutation. It was thought at first that this was due to the formation of hydrogen peroxide. This theory, being disproven, was abandoned, but since irradiation by ultraviolet light formed organic peroxides, on certain culture plates, attention was shifted to them as the possible agents of the mutation induction.

Spores from a pure strain of adinene-dependant bacteria, upon being immersed in water solutions of various organic peroxides, formed bacterial cultures which were adinene-independant. These adinene-independant bacterial cultures were located by inoculating the treated spores on adinene-free plates. Proof that gene mutations are involved can only be obtained by the study of genetic crosses involving bacteria from these cultures.

The mutations produced by organic peroxides are similar, in very many respects, to those produced by other chemical mutagens and by

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[17]Auerback, Charlotte, Chemical Mutagenesis, Cambridge Philisophical Society Biological Review, 24(1949) 386.

radiational mutagens. The fact that media, used in bacterial cultures, when irradiated with ultraviolet first cause mutations, gives support to the theory that ultraviolet light irradiation produces mutations by forming peroxide compounds. Because mutagenic agents are so similar, in types and numbers of mutations produced, some scientists believe that all mutagens, regardless of the type, have in common a way of producing mutations. If this is the case mutagens such as X-rays and nitrogen mustard, may be dependant upon peroxide formation in their mutation production.[18]

A great deal of work has been done in chemical mutagenesis, but one might say the field is still in its infancey. A large number of chemical compounds, including salts, ethers, acetone, acids, etc., have been tested. Only a relative few substances have been found with definate mutagenic properties, and most of these have been listed above.

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[18]Dickey, Frank H., "The role of organic peroxides in the Induction of Mutations, National Acadamy of Sciences Proceedings, 35(1939),pp.581-586.

Chapter IV

MUTATIONS WHICH AFFECT MAN

Almost all mutations, occuring in any organism, are of a harmful nature. The degree to which they are detrimental may range from a disability so slight it may not even be noticable, to one so severe it causes death. It is exceedingly difficult to say that such a change, or the appearance of beneficial changes in man is due to mutation because of man's heterozygous nature. Some changes, particularly the harmful ones, are so striking in nature, and so persistant in reoccurance in future generations, that geneticists are best able to explain them in terms of mutation. It is the purpose of the writer to survey a few examples of such mutations, in order to gain a knowledge of them.

A mutation which had far reaching effects on her decendents, is believed to have occured in Victoria, Queen of England. Geneticists now believe that a recessive sex-linked mutation occured in her reproductive organs which produced a gene for the disease, hemophilia. Historians have not been able to find a record of any of her ancestors as having had the disease; however of her children, one son and two daughters were either suffers or carriers of the disease.[1] One son, Leopold, passed the gene to his daughter who was a carrier. Alice, her second daughter and a carrier, was to become the grandmother of Alexis Tsarevitch of Russia, a sufferer of hemophilia. The other carrier daughter,

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[1]Colin, Edward Elements of Genetics (Philadelphia,1946) p. 245.

Beatrice, produced a carrier daughter Eugenie, wife of Alfonso XIII of Spain. This union produced two sons who were hemophilics, including the crown prince. Who can tell but what the presence of hemophilia in the crown princes of both Russia and Spain had a great deal to do with the overthrow of both dynasties? Scientists are sure the condition arose by mutation, for no other possible explanation can be found.

Another mutation, harmful to man, is Ehlers-Danlos syndrome. A person afflicted with this disease shows a number of symptoms. The joints are so loose and limber that the thumb of such a person can be easily bent backwards to touch the lower arm. An even more serious characteristic is the extreme fragility of the blood vessels beneath the skin. This allows many small ruptures in these vessels and hence frequent hemorrhages.

A mutation, called the mono-digital mutation, causes a most disabling effect in man. Such a mutation is characterized by a fusion of the finger and toe bones; the result often looks much like the claw of a lobster, from which the common name of "lobster claw" is derived. The severity of the condition ranges from this to the mere absence of a thumb or finger nail. The crippling effect of this mutation, in severe cases, is so great that many people consider it improper to permit an afflicted person to produce offspring.

A recessive mutation occuring in man, is the mutation causing a gene to give the characteristics of albinism. Since it is a recessive character, both parents must have undergone a mutation or received a mutant gene from their ancestors in order for their offspring to express the characteristic. In our modern civilization, such a mutation is not particularly harmful since such a person can easily protect himself from an

excess of sunlight. A case of albinism in a person who is constantly subjected to large amounts of sunlight would more than likely produce fatal results. Without the normal pigments in the body, a person is so sensitive to light that it causes squinting even when greatly reduced in quantity.

Mankind, as other organisms, is afflicted with lethal mutations. These are mutations which produce death before, at, or soon after birth. In a few cases, such a mutation may produce a condition that will not cause death until after the individual is several decades old. The time interval, of course, depends on the mutation, and the severity of the disease caused.

A mutation causing a defect in an embroyo's heart, kills the embryo, and causes a miscarriage. A mutation affecting a organ not to be used until birth, will not cause death until such a time as the child is severed from the umbilibal cord.

An example of a lethal mutation is the one causing the recessive character of Brachyphalangy. This disease is characterized by having only two joints per finger. If a person has this, it indicates that he or she has received a mutant gene from one parent. When two such people marry, they can expect one-fourth of their children to have normal hands, one-fourth to have Brachyphalangy, and one-fourth to die as infants. Children possesing two mutant recessive genes have extreme skeletal deformities and cannot live because of them.

Many other defects such as night blindness, extremely brittle bones, defects of the skin, skeleton, muscular system, and countless others are all types of human defects produced by mutation. These illnesses and defects are a menace to the human population as a whole; new mutations

are continually arising, and the old ones are being transmitted to offspring. Many people have wondered what could be done about the situation and decided it was hopeless. Others believe in and demand the use of Eugenics. This is a system whereby defective persons are rendered sterile, or even destroyed. Perhaps sterilization in some cases is a partial answer; but the taking of human lives, is no solution to any problem.

Mutations affect all living organisms the world over, and as in human beings, the majority of these are of a harmful nature. An example of these harmful ones is the case of the Dexter cattle. Dexter cattle are better beef producers than a similar breed the Kerry. Breeders learned that it is not profitable to cross Dexter Cattle. The characteristics of the Dexter breed are the result of a heterozygous recessive mutant gene which acts as a lethal in the homozygous condition. This means that when Dexters are crossed, the ratio of offspring is one Kerry; two Dexters; one Bulldog. The Bulldog calf if so named because of extremely short legs and a bulldog-like muzzle. Bulldog calves usually are still-born or else die within a day or so. An other example of a harmful mutation among animals is the creeper chicken. Creeper chickens have extremely short legs, on which they creep rather than walk. This condition decreases the chickens potential as an egg and meat producer. Man is more interested in beneficial mutations than with harmful ones among his stock animals, for by utilizing those few which show new desirable characteristics, he can upgrade the quality of all his animals of that breed.

Examples of beneficial mutations which man has found and used are the Santa Gertrudis cattle and the Ancon sheep. There are many more

examples which could be given, but these two will illustrate.

Ancon sheep were first originated in the late eighteenth Century by a New England farmer. The forerunner of this breed appeared in his flock, and was characterized by extremely short legs. By breeding from it, the farmer developed a breed of sheep with legs so short they could not jump over stone fences. Some fifty or sixty years later, a Norwegian farmer developed a strain of short legged sheep in the same manner. To farmers depending on stone fences to enclose their animals this type sheep was an improvement.

Santa Gertrudis cattle were developed on the King Ranch in Texas. Trying to develop a strain of cattle to withstand heat, dry weather, and ticks, the rancher had been trying crosses primarily between shorthorn and brahma cattle. There appeared in the herd, a red bull calf, so peculiar in appearance that he was named "Monkey". As he grew older, the rancher noticed he had admirable beef-producing qualities. As soon as possible, he bred from him the first of the Santa Gertrudis cattle. By capitilizing on a mutant calf, the King Ranch was able to develop a breed of cattle recognized the world over as being particularly well suited for the production of beef in a hot, dry, climate.

In like manner, a number of new strains of plants have been developed from newly appearing mutant forms. Also, a great many harmful mutations, such as albino plants, have appeared. Albinism, as in corn, is a lethal mutation. The young plant can live only as long as its stored food lasts, for lacking cholorophyll, it cannot synthesize any food.

Mutations have given rise to new strains of crops which are resistant to drowth, wind, and disease. By breeding true, these strains have enabled man to produce crops in areas where before it had been impossible

to do so. This of course has increased man's ability to produce greater yields with less efforts.

Some mutations in the plant Kingdom merely increase the quality of an already important crop. Examples of this latter case are the seedless Emperor grapes, and the navel oranges. The yellow delicious apple is believed to have originated in a similar way. It has been found, that of necessity, the mutants producing seedless fruits must be propagated by grafting or budding. So it is that one branch or limb of a plant that experiences a mutation which is beneficial to man, may be used to propagate thousands of plants with similar characteristics.

These few examples show how mutations acting on plants and animals may deeply influence the mode of Man's life.

Chapter V

CONCLUSION

Many people have spent large amounts of time and effort to find satisfactory explanations for mutation causation. In spite of this fact most authorities in the field feel that questions about mutations have not yet been answered satisfactorily. Man is now entering an age of advancing technology which will doubtless bring satisfactory answers for many of the remaining questions. The use of perfected radiological technique will hold the key to many problems now confronting investigators in this work, as well as the improvement of laboratory techniques which have previously proven fruitful.

This report does not contain all the information that is presently known concerning mutation, and it is not in any sense, a detailed scientific account of what is known of the areas with which the report deals. An attempt has been made to present facts and answer questions about mutations in such a way that people lacking a scientific background can understand it readily. The major points considered in the report were concerned with the causation of mutations and also the effects which the mutations have on man and his domesticated organisma.

The literature consulted for this report does not offer any convincing explanation as to the causes of mutations. Two theories, common to most of the literature, concerning the causes of mutations are those of ionizing particles and of peroxide formation. Considerable evidance has been given that these two factors may work in connection with one another to

bring about mutation. Since such a relatively small bit of knowledge has been gathered heretofore, only time and the information it will afford will give the complete and true answers to these questions.

Man is able to see more easily the effects of mutation than he is the causes. He is able to recognize improvement in his domesticated plant and animal strains. Man has been able to see how some mutations may even affect him directly. Many effects of mutations doubtless slip by Man's unseeing eyes and the mutation is never recorded or studied. With the advent of better understanding, the effects of mutations will become even more pronounced.

SELECTED BIBLIOGRAPHY

Auerbach, Charlotte, "Chemical Mutagenesis," Cambridge Philisophical Society Biological Review, XXIV, July, 1949, p. 355.

Biological Principles and Concepts for High School Science Teachers, 1957, p. 21-13.

Colin, Edward, Elements of Genetics. Philadelphia: The Blakiston Company, 1946.

Dickey, Frank H., "The Role of Organic Peroxider in the Induction of Mutations," National Acadamy of Sciences Proceedings, XXXV, September, 1939, p. 581.

Demerec, E. and Latarjet, R., "Induced Mutation in Bacteria," Cold Spring Harbor Symposia on Quantatative Biology, XI, 1941, p. 38.

DeVries, Hugo, The Mutation Theory, Vol. II. Chicago: The Open Court Publishing Company, 1910.

Dodson, Edward, Genetics. Philadelphia: W. B. Saunders Company, 1956.

Elliot, Hugh, Tr., Zoological Philosophy. London: MacMillan and Company, 1914.

Gabriel and Fogel, Ed., Great Experiments in Biology. Englewood Cliffs: Prentice Hall, Inc., 1955.

Hollaender, Alexander, Ed., Radiation Biology, Vol. I. New York: McGraw-Hill, 1954.

Horlacher, W. R., "An Attempt to Produce Mutation by Use of Electricity," Science, LXXII, July, 1930, p. 96.

Muller, H. J., "Genetic Damage Produced by Radiation." Science, CXXI, July, 1955, p. 837.

Packard, A. S., Lamark, His Life and Work. New York: Longmans, Green and Company, 1901.

Sinnot, Dun, and Dobzhansky, Principles of Genetics. New York: McGraw-Hill, 1950.

Winchester, A. M., Heredity and Your Life. New York: Vantage Press, 1956.

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